Amendments to the Specification:

Please delete the paragraph on page 4, lines 27-29.

Please replace paragraph the paragraph at page 8, lines 15-30 with the following amended paragraph:

FIG. 8. The hepatic gene expression profiles of old control, old CR, young control, and young CR mice. The mice weighed 37.2+1.9 g, 22.8+1.2 g, 26.0+2.8 g, and 19.4+1.6 g, respectively. The CR groups consumed approximately 50% fewer calories than their control counterparts post weaning, as described. Levels of specific mRNA were determined using the Mu11KsubA and Mu11KsubB ~~GeneChip~~ GeneChip® arrays (Affymetrix, Santa Clara, CA) containing targets for approximately 12,000 known mouse genes and ESTs. The experiment tree function of GeneSpring 3.0 (Silicon Genetics, San Carlos, CA) was utilized to display the results. The horizontal axis represents the position of each gene assigned by the "gene tree" average linkage hierarchical clustering algorithm of the program. ~~Below the position assigned to each gene is a color coded indication of its relative expression level, based on a continuous scale. Bright blue indicates no detectable expression, purple average expression, and bright red high expression. The average expression of each gene in each group is shown.~~ The GeneSpring "experiment tree" clustering algorithm calculated an average-linkage hierarchical clustering dendrogram of the data for each group of mice, which is shown to the left of the expression profiles.

Please replace paragraph the paragraph at page 9, lines 15-28 with the following amended paragraph:

FIG. 11. The hepatic gene expression profiles of young CR, young control and streptozotocin (STZ)-treated mice. Levels of specific mRNA were determined using the

Mu11KsubA and Mu11KsubB ~~GeneChip~~ GeneChip® arrays (Affymetrix, Santa Clara, CA) containing targets for approximately 12,000 known mouse genes and ESTs. The experiment tree function of GeneSpring 3.0 (Silicon Genetics, San Carlos, CA) was utilized to display the results. The horizontal axis represents the position of each gene assigned by the "gene tree" average linkage hierarchical clustering algorithm of the program. ~~Below the position assigned to each gene is a color coded indication of its relative expression level, based on a continuous scale. Bright blue indicates no detectable expression, purple average expression, and bright red high expression.~~ The average expression of each gene in each group is shown. The GeneSpring "experiment tree" clustering algorithm calculated an average linkage hierarchical clustering dendrogram of the data for each group of mice, which is shown to the left of the expression profiles.

Please replace paragraph the paragraph at page 10, lines 1-14 with the following amended paragraph:

FIG. 13. The hepatic gene expression profiles of old CR, old control and aminoguanidine (Au) treated mice. Levels of specific mRNA were determined using the Mu11KsubA and Mu11KsubB ~~GeneChip~~ GeneChip® arrays (Affymetrix, Santa Clara, CA) containing targets for approximately 12,000 known mouse genes and ESTs. The experiment tree function of GeneSpring 3.0 (Silicon Genetics, San Carlos, CA) was utilized to display the results. The horizontal axis represents the position of each gene assigned by the "gene tree" average linkage hierarchical clustering algorithm of the program. ~~Below the position assigned to each gene is a color coded indication of its relative expression level, based on a continuous scale. Bright blue indicates no detectable expression, purple average expression, and bright red high expression.~~ The average expression of each gene in each group is shown. The GeneSpring "experiment tree" clustering algorithm calculated an average linkage hierarchical clustering dendrogram of the data for each group of mice, which is shown to the left of the expression profiles.

Please replace the paragraph at page 25, lines 16-23 with the following amended paragraph:

~~GeneChip o~~Oligonucleotide based high-density array RNA expression assays were performed according to the standard Affymetrix protocol. The biotinylated, fragmented cRNA was hybridized to the Mu11KsubA and Mu11KsubB ~~GeneChip~~ GeneChip® arrays (Affymetrix, Santa Clara, CA), which contain targets for more than 11,000 known mouse genes and ESTs. The arrays were washed, stained and scanned. Scanned image analysis and data quantification were performed using the Affymetrix ~~GeneChip~~ GeneChip® analysis suite v3.2 at default parameter settings. Resultant data were normalized by global scaling.

Please replace the paragraph at page 28, line 20 bridging to page 29, line 7 with the following amended paragraph:

Table 2 shows the number of genes and expressed sequence tags (ESTs) in each of the other groups. Ninety percent of these genes and ESTs were in the high-low-high and low-high-low groups. In these groups, the short- and long-term CR expression patterns are most similar. The other 4 groups accounted for only 10% of the remaining genes and ESTs. These data indicate that short- and long-term CR produced remarkably similar effects on the expression of more than 11,000 hepatic genes and ESTs. A complete listing of the expression data for the genes and ESTs in each group is available. ~~(http://www.biochentistry.ucr.edu/faculty/spindler.html/GeneChipData) (This URL will be activated upon allowance of this application).~~

Please replace the paragraph at page 47, line 30 bridging to page 48, line 11 with the following amended paragraph:

We have tested the hypotheses that CR produces similar effects on gene expression early and late in life by examining the effects of aging and caloric intake on the expression of approximately 12,000 genes and ESTs in the liver of old (27 month-old) and young (7

month-old), control and CR mice, using ~~GeneChip~~ oligonucleotide based high-density microarrays. We found that CR produced a massive reprogramming of gene expression early and late in life. The patterns of expression induced by CR in young and old mice were highly homologous. Comparison of gene expression in the groups of mice indicated that CR only prevented age related changes in the expression of a few genes. Examination of the genes involved does not support the idea that they have a principle role in the age-retarding effects of CR. Together, the results do not support the idea that CR acts principally to prevent deleterious age related changes in gene expression. Instead, CR induces a highly homologous, major reprogramming of gene expression in animals of all ages.